A Patient with Jaundice and Pruritus, Not the Usual Suspect?

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To

Howard M. Peek, Jr.
Douglas A. Corely
Editors in chief of Gastroenterology

Date 29 January 2019
Subject Cover letter for submitted manuscript Meijer *et al.*

Dear editor,

We hereby submit the accompanying manuscript entitled *Pruritus in a patient with jaundice, not the usual suspect?* by Meijer *et al.* to be considered for publication as 'Clinical Challenge' in Gastroenterology.

Pruritus is a common condition associated with jaundice. Here, we present a clinical case of a patient with jaundice and pruritus due to yellow urticaria: a learning point that pruritus is not always caused by the usual suspect. Yellow urticaria can be observed with the presence of urticaria in a patient with jaundice, due to excessive bilirubine deposits in the skin. Only eleven cases of yellow urticaria have been reported so far, this is the first case of yellow urticaria due to autoimmune hepatitis. With this clinical challenge, we would like to emphasize the importance of skin examination of patients with jaundice. Although urticaria can be well recognized, yellow urticaria is probably underrecognized in clinical practice. Treatment is succesfull with antihistamines, as illustrated in this case.

All data are original and have not been published elsewhere. All authors have read and approved the manuscript, its content, and its submission to Gastroenterology. The authors state no conflict of interest.

On behalf of the authors, with kind regards,

Joost M. Meijer MD PhD
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A patient with jaundice and pruritus, not the usual suspect?

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Question: A 43-year old, previously healthy man developed jaundice, tiredness and intense pruritus. Symptoms started three days before presentation and included dark colored urine. He had no complaints of pain, nor fever. He had no history of alcohol use or substance abuse. The only medication used was ciprofloxacin (urinary tract infection) for 14 days six weeks prior to onset of symptoms. On physical examination there was conjunctival icterus and slight jaundice, with several edematous yellow plaques with an erythematous border distributed accross the arms, upper legs (**Figure A**) and dorsal side of the feet (**Figure B**). Blood tests revealed a total bilirubin of 154 umol/L (upper limit, 17), direct bilirubin 138 umol/L (upper limit, 5), aspartate aminotransferase 748 U/L (upper limit, 40), alanine aminotransferase 1813 U/L (upper limit, 45), and alkaline phosphatase 133 U/L (upper limit, 120). He showed no signs of acute liver failure. Abdominal ultrasound imaging showed no abnormalities, with no signs of cholelithiasis. The severe pruritus led to nocturnal distress and intense scratching. After start of treatment his complaints of pruritus and the skin lesions resolved within two days, without recurrences.

Based on these clinical symptoms, physical examination and laboratory findings, what is the most likely diagnosis of his pruritus?

Answer: Our patient's symptoms of pruritus and acute pruritic, slightly elevated erythematous papules or plaques (wheals) are illustrative of urticaria, also known as hives. Lesions appear transient and resolve in less than 24-48h. In the unusual variant of yellow urticaria, the yellow discolorisation is associated with high bilirubin levels and bilirubin skin deposits due to diverse liver diseases.[1] Eleven cases have been reported in literature, with related infective hepatitis, alcohol induced liver disease, cirrhosis, acute liver failure, and metastatic disease to the liver (breast).[1] Clark first described yellow urticaria in 1969 during jaundice in a patient with infectious hepatitis, with remission of the urticaria after the hepatitis resolved.[2] In our patient a differential diagnosis was considered of drug-induced toxic hepatitis and auto-immune hepatitis. The latter was diagnosed after liver biopsy. Awaiting further diagnostic testing, the urticaria was treated with the antihistamine desloratadine 5mg up to four times a day, and could be tapered within two days after remission of the pruritus. Having been diagnosed with auto-immune hepatitis the patient received prednisolone 30mg a day, which was tapered after clinical remission and with normalization of liver tests.

A more intense yellow color can be observed in the urticarial lesions compared to jaundice as is usually seen (**Figure B**), which might occur due to capillary vasodilatation and plasma extravasation that leads to increased bilirubin deposits in the urticarial lesions.[1,3] A skin biopsy of the urticarial lesions may only show dermal edema, bilirubin depositions in the dermis can be stained with Hall's staining (not available).[3] Jaundice and the yellow discolorisation of urticaria may persist for several days after normalization of bilirubin level, due to the high affinity of bilirubin for elastin in the skin. Urticaria may be induced by various factors such as infections, allergens, autoimmunity or drugs. Cases of yellow urticaria have been reported in patients with a predisposition to urticaria.[3] However, our patient had no previous history of urticaria. The high prevalence of urticaria raises the question, whether yellow urticaria might be a more common skin manifestation in patients with jaundice and pruritus than reported.

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FIGURES

Figure A

Figure legend

Figure A – A raised yellow urticarial plaque on the upper leg with an erythematous border and linear scratch marks, with a slight jaundice of the surrounding skin.

Figure B

Figure legend

Figure B – Localized yellow plaque of the skin on the dorsal side of the left foot with an erythematous border. Intensity of yellow discolorisation increased after pressure on the skin by the patient.

Figure A

Click here to access/download;Figure;Figure A.jpg

Figure B

Click here to access/download;Figure;Figure B.jpg